SM

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,557	05/24/2001	David Beach	GNCA-P02-007	4804

28120 7590 07/09/2004

ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 07/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,557	BEACH ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9,10 and 12-42* is/are pending in the application.

4a) Of the above claim(s) *16-25 and 30-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9,10,12-15 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/6/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's preliminary amendment filed on January 3, 2004 is acknowledged and has been entered.

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1, 3-4, 9-10, 12-15 and 26-29 in the reply filed on May 3, 2004 is acknowledged. The traversal is on the ground(s) that Group I is closely related to the claims of Group VI which are directed to an isolated guide RNA, while the claims of Group I are directed to a method for attenuating expression of a target gene using the guide RNA of the Group VI. Applicants submit that simultaneous examination of the pending claims of Groups I and VI will not impose a substantial additional burden on the Examiner. Applicant quotes a citation from MPEP 803 and states that there is no significant additional burden on the examiner to search Group VI together with the elected Groups I. Applicant concludes that reconsideration and withdrawn of the restriction requirement are respectfully requested. The arguments have been thoroughly reviewed and considered. However, this is not found persuasive because the different inventions listed as Groups I-VII are distinct because they have separate modes of operation, separate functions and results in separate effects. Furthermore, the different inventions would constitute an undue search burden to the Examiner because the different invention would require searching separate and non-overlapping areas if not restricted. For example, a search of the subject matter of Group VI on one commercial database revealed over 6000 prior art documents. Additionally, it is believed that the searches for the different inventions are not co-extensive because an isolated guide nucleic acid as recited in Group VI can be used in a materially different process besides in the method of Group I. The

product of Group can be used as a primer in nucleic acid amplification procedures or in methods of nucleic acid cloning procedures or alternatively, the product can be further processed and used as a therapeutic compound or an anti-cancer agent. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1, 3, 4, 9, 10, 12-42 are pending. Claims 16-25 and 30-42 are withdrawn from consideration as being drawn to a non-elected subject matter. Claims 1, 3, 4, 9, 10, 12-15 and 26-29 are discussed in this Office Action.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application *(60/189,739, filed on March 16, 2000)* upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1, 3-4, 9-10, 12-15 and 26-29 of this application. Specifically, the provisional application 60/189,739 filed on March 16, 2000 does not provide support for the limitation recited in claim 1, wherein "the dsRNA comprises a complementary nucleotide sequence of 20-50 nucleotides that hybridizes under... to a portion of the target gene". The provisional application discloses the use a double stranded RNA comprising a complementary sequence within the range of 50-800 nucleotides in length. The provisional application additionally teaches that the dsRNAs comprising sequences within the range of 50-100 nucleotides in length were inert in their assays for attenuating expression of a target gene. No support was found anyway in the provisional application to support the limitations of a double stranded nucleic acid comprising a complementary nucleotide sequence within the range of 20-50 nucleotides in length that hybridizes under stringent

conditions to a portion of a target gene. Therefore in view of the foregoing, priority has not been granted for provisional application 60/189,739.

Drawings

4. Applicant's submission of formal drawings was received on January 2, 2003. The formal drawings are acceptable.

Specification

5. The disclosure is objected to because of the following informalities:

(a) The specification is objected to at page 3, first paragraph and page 17, second paragraph because the designation for the sequence identifier is improper (see MPEP§ 2422.03). It is suggested amending the disclosure to recite --SEQ ID NO:--.

(b) The specification is objected to at the "Brief Description of the drawings" beginning on Page 6 because the description disclosed in the specification for Figures 1, 2, 4, 8, 20 and 22 does not coincide with the formal drawings received on January 2, 2003. For example, in Figure 1, the legend labels are not the same. The specification recites a, b, and c, whereas, the formal drawing for Figure 1 recites 1A, IB and 1C. In Figure 2, the same discrepancy applies as stated for Figure 1. Additionally, the formal drawing for Figure 2 depicts a Fig. 2D, which is not described in the specification at page 6. In Figure 4, the legend labels are not the same as depicted in the formal drawings. The specification for Figure 4 recites a, and b, whereas, the formal drawings recites A and B. In Figure 8, the specification recites a figure C, however, no Fig. 8C is disclosed in the formal drawings. In Figure 20, the formal drawing depicts Figures 20A, 20B and 20C, however, the specification provides no description or recite a Figure 20A-C.

The same applies for figure 22. The formal drawing depicts a Figure 22A and 22B, however, the specification provides no description of a Figure 22A and 22B.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 15 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for attenuating expression of a target gene in a cell, wherein said expression of the target gene is attenuated up to 7.4 fold, it does not reasonably provide enablement for a method for attenuating expression of a target gene in a cell, wherein said expression of the target gene is attenuated by at least 10 fold. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See In re Wands, 858 F. 2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)). These factors include, but are not limited to: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented in the specification, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the

unpredictability of the art and (8) the breadth of the claims. Claim 15 is drawn to an embodiment of claim 1, wherein expression of the target gene is attenuated by at least 10 fold. The specification teaches at 3 of the specification beginning at line 27 that "in certain preferred embodiments, expression the target gene is attenuated by at least 5 fold, and more preferably at least 10, 20 or even 50 fold, e.g., relative to the untreated cell or a cell treated with a double stranded RNA construct which does not correspond to the target gene. At page 8, beginning at line 23 and Figure 7, the specification demonstrates wherein the expression of the target gene is attenuated by 7.4 fold and 6.2 fold. At page 22 in the first and third paragraphs, the specification discloses wherein the expression of a target gene is attenuated by 6-7 folds. Nowhere in the specification does applicant demonstrate wherein a target gene is attenuated by at least 10 folds. There are no working examples or direction given that would suggest that the method is capable of attenuating a target gene by at least 10 fold or higher. Merely making reference that the expression of a target gene can be attenuated by at least 10, 20 or even 50 fold relative to the untreated cell or a cell treated with a dsRNA construct which does not correspond to the target gene as being encompass by the invention does not enable the practitioner to reproduce the results as reported for the broad scope of the claimed invention. The specification does not disclose a method as claimed in claimed 15 that bears a reasonable correlation to the entire scope of the claim. Therefore, one skilled in the art would not know how to make or use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112 second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 3-4, 9-10, 12-15 and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1, 3-4, 9-10, 12-15 and 26-29 are indefinite at "stringent conditions" because the term "stringent" is not defined in the specification or claims and it cannot be determined what hybridization conditions are required for the method to operate. Clarification is required.

(b) Claim 27 lacks proper antecedent basis for "said complementary guide sequences" because claim 1 from which is depends does not recite "complementary guide sequences" but recites "complementary sequences". It is suggested amending the claim such that the claims languages agree.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1, 3-4, 9-10, 12-14, 26, 27 and 29 rejected under 35 U.S.C. 102(e) as anticipated by Li et al (US 2002/0114784 effective filing date January 2000). Regarding claim 1, Li et al teach a method for attenuating expression of a target gene in a mammalian cell, comprising

introducing a double stranded RNA (dsRNA) into the cell in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a complementary nucleotide sequence of 25-100 nucleotides in length that hybridizes to a portion of the target gene (see paragraphs (0006, 0028-0039,).

Regarding claim 3, Li et al teach the method of claim 1, wherein the cell is suspended in culture (0006).

Regarding claim 4, Li et al teach the method of claim 1, wherein the cell is in a whole animal, such as a non-human animal (0006 and 0033).

Regarding claim 9, Li et al teach the method of claim 1, wherein the target gene is a genomic gene if the cell (0032).

Regarding claim 10, Li et al teach the method of claim 1, wherein the target gene is an heterologous gene relative to the genome of the cell, such as a pathogen gene (0032).

Regarding claim 12, Li et al teach the method of claim 1, wherein the cell is a primate cell (0033).

Regarding claims 13 and 29, Li et al. teach the method of claim 1 and 13, wherein the dsRNA is about 20 nucleotides in length (clm 13) or about 22 nucleotides in length (0039).

Regarding claim 14, Li et al teach the method of claim 12, wherein the cell is a human cell (0033).

Regarding claim 26, Li et al teach the method of claim 1, wherein the dsRNA is produced by a vector (0041).

Regarding claim 27, Li et al teach the method of claim 1, wherein the dsRNA is a hairpin RNA including the complementary sequence (0036-0038). Therefore, Li et al meets the limitations of claims 1, 3-4, 9-10, 12-14, 26, 27 and 29 of the instant invention.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 3-4, 9-10, 12-15, 26-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 8-9, 13-18 and 20 of U.S. Patent Application 10/350,798 (prePUB NO: US 2004/0086884). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 2, 8-9, 13-18 and 20 of U.S. Patent Application 10/350,798

(prePUB NO: US 2004/0086884) are generic to the species of the invention covered by claims 1, 3-4, 9-10, 12-15, 26-29 of the instant invention. That is, the claims 1, 2, 8-9, 13-18 and 20 of U.S. Patent Application 10/350,798 (prePUB NO: US 2004/0086884) falls entirely within the scope of the claims 1, 3-4, 9-10, 12-15, 26-29 of the instant invention. As the court stated in *In re Goodman*, 29 USPQ2d 2010 (CAFC 1993), " a second application-- "containing a broader claim, more generical in its character than the specific claim in the prior patent"--typically cannot support an independent valid patent. Miller, 151, U.S. at 198; See Stanley, 214 F.2d at 153. Thus, the generic invention, as noted above is "anticipated" by the species of the patented invention. Cf., Titanium metal corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (holding that an earlier species disclosure in the prior art defeats any generic claims). This court's predecessor has held that, without a terminal disclaimer, the species claims preclude issuance of the generical application. "*In re Van Ornum*, 686 F.2d 937, 944, 214 USPQ 761, 767 (CCPA 1982); *Schneller*, 397 F.2d at 354".

14. Claims 1, 3-4, 9-10, 12-15, 26-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 10, 11, 12-13, and 15 of U.S. Patent Application 09/858,862 (prePUB NO: US 2004/0018999). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (fed. Cir.

1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3, 4, 10, 11, 12-13, and 15 of U.S. Patent Application 09/858,862 (prePUB NO: US 2004/0018999) are generic to the species of the invention covered by claims 1, 3-4, 9-10, 12-15, 26-29 of the instant invention. That is, the claims 1, 3, 4, 10, 11, 12-13, and 15 of U.S. Patent Application 09/858,862 (prePUB NO: US 2004/0018999) falls entirely within the scope of the claims 1, 3-4, 9-10, 12-15, 26-29 of the instant invention. As the court stated in *In re Goodman*, 29 USPQ2d 2010 (CAFC 1993), " a second application-- "containing a broader claim, more generical in its character than the specific claim in the prior patent"--typically cannot support an independent valid patent. Miller, 151, U.S. at 198; See Stanley, 214 F.2d at 153. Thus, the generic invention, as noted above is "anticipated" by the species of the patented invention. Cf., Titanium metal corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (holding that an earlier species disclosure in the prior art defeats any generic claims). This court's predecessor has held that, without a terminal disclaimer, the species claims preclude issuance of the generical application. "*In re Van Ornum*, 686 F.2d 937, 944, 214 USPQ 761, 767 (CCPA 1982); *Schneller*, 397 F.2d at 354".

15. Claims 1, 3-4, 9-10, 12-15, 26-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 14-20 of U.S. Patent Application 10/055,797 (prePUB NO: US 2004/0084471). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g.,

In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-3, 14-20 of U.S. Patent Application 10/055,797 (prePUB NO: US 2004/0084471) are generic to the species of the invention covered by claims 1, 3-4, 9-10, 12-15, 26-29 of the instant invention. That is, the claims 1-3, 14-20 of U.S. Patent Application 10/055,797 (prePUB NO: US 2004/0084471) falls entirely within the scope of the claims 1, 3-4, 9-10, 12-15, 26-29 of the instant invention. As the court stated in *In re Goodman*, 29 USPQ2d 2010 (CAFC 1993), " a second application-- "containing a broader claim, more generical in its character than the specific claim in the prior patent"--typically cannot support an independent valid patent. Miller, 151, U.S. at 198; See Stanley, 214 F.2d at 153. Thus, the generic invention, as noted above is "anticipated" by the species of the patented invention. Cf., Titanium metal corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (holding that an earlier species disclosure in the prior art defeats any generic claims). This court's predecessor has held that, without a terminal disclaimer, the species claims preclude issuance of the generical application. "*In re Van Ornum*, 686 F.2d 937, 944, 214 USPQ 761, 767 (CCPA 1982); *Schneller*, 397 F.2d at 354".

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-

0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Cynthia Wilder

CYNTHIA WILDER
PATENT EXAMINER

7/6/2004